

1. The prior art contains all of the claimed features, however, not in one single document.
2. The skilled artisan would combine these features (from different documents).
3. The skilled artisan would expect the results as being obvious.

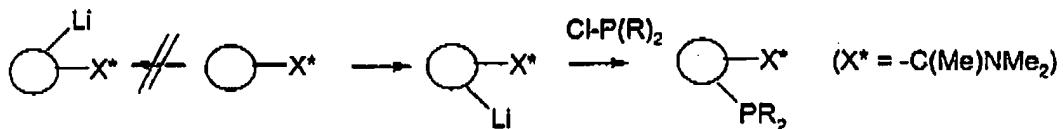
Re 1. The prior art contains all claimed features, however, not in one single document

The arguments by the Examiner presented in the Office Actions of May 29, 2009 and January 4, 2010 with regard to the claimed features are interpreted as follows:

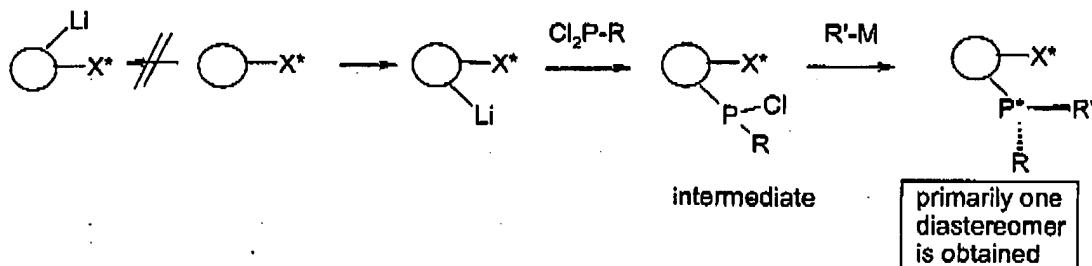
- Hayashi et al. teach the ortho-lithiating step.
- Hayashi et al. teach as the result of said step a phosphine having identical radicals (-PRR).
- The instant application teaches chiral phosphines (-PRR', where R is not equal to R') obtained by nucleophilic addition of R'-M to an intermediate -PCIR.
- The **difference** is: Hayashi et al. disclose non-chiral phosphines, whereas the instant application discloses chiral phosphines.
- Nettekoven et al. teach ferrocene catalysts having chiral phosphine ligands.
- Nettekoven et al. teach that said catalysts are useful for catalytic asymmetric allylic substitution reactions.
- Berlin et al. teach the possibility of applying a Grignard reaction for introducing a group R onto a phosphine, where group R is different from the phenyl groups of diphenylphosphine chloride.

Nettekoven et al. disclose a totally different method from that of the present invention for preparing chiral phosphine ligands, and is cited for the teaching of the usefulness of chiral phosphine ligands. Thus, Nettekoven et al. disclose the feature "chiral phosphine groups", however, is otherwise unrelated to the instant preparation process. Therefore, only the teachings of Hayashi et al. and Berlin et al. and the instant invention are summarized in the following schemes:

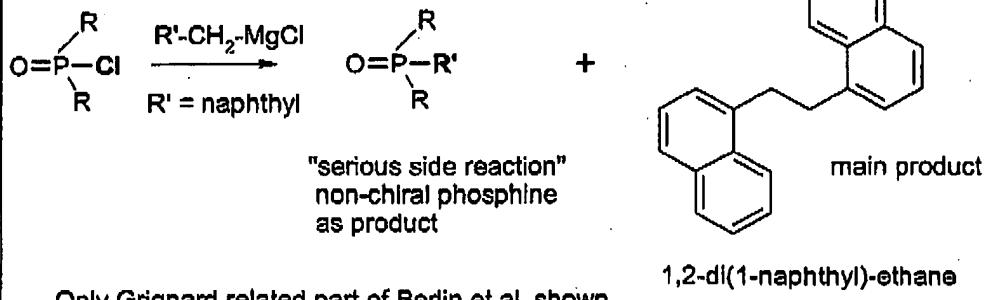
Hayashi et al.:



Instant application:



Berlin et al.: Grignard versus Michaelis-Arbuzov Rearrangement:



The differences:

- Hayashi et al. do not disclose the feature of the instant **intermediate** compound.
- Berlin et al. teach only that a phosphine chloride can be reacted with RMgCl, however the phosphor compound is a **P(V)-compound** and not a **P(III)** compound and the resulting product of the "serious side reaction" is **not a chiral compound**.

- It should be noted that so far the Examiner has failed to show where the feature "formation of the instant intermediate" (reaction with  $\text{Cl}_2\text{PR}$  instead of the reaction with  $\text{Cl-P}(\text{R})_2$  according to Hayashi et al.) can be found in the references. Consequently, the requirement under point 1 above, namely that the cited prior art contains all claimed features, is currently not fulfilled by the Examiner.

## 2. The skilled artisan will be able to combine these features (from different documents)

Since one feature of the present invention, i.e. the intermediate, is missing from the prior art, a combination of the prior art features can not lead to the present invention. Further, the product of the Grignard reaction according to Berlin et al. does not result in a chiral phosphine. Nevertheless, the Examiner combines the teachings of Hayashi et al. and Berlin et al., which is improper.

## 3. The skilled artisan would expect the results as being obvious

"Being obvious" would mean that the skilled artisan would expect that using the method of the present invention **leads to the formation of primarily one of more than one possible diastereomers with high diastereoselectivity, i.e. enables the art-skilled to prepare P-chiral phosphines with high stereoselectivity.**

However, such expectation can not be derived from the cited prior art as explained below.

According to the Examiner there is motivation for the skilled person to make the instant invention by applying the teachings of Hayashi et al., Nettekoven et al. and Berlin et al.

The line of argumentation of the Examiner is interpreted again as follows:

- Nettekoven et al. show that chiral phosphines can be useful, thus, there is motivation for formation of chiral phosphine ligands.
- Hayashi et al. show possible formation of non-chiral phosphines.
- Berlin et al. teach a possible way of preparing non-chiral phosphines by introducing a group R' onto a phosphine (V) chloride via a Grignard reaction.
- Motivated by Nettekoven et al. to prepare chiral phosphine ligands, it would be obvious to apply the method as disclosed by Berlin et al. for introducing a different group R onto the non-chiral phosphine obtainable according to the disclosure of Hayashi et al. (despite the fact

that there is neither an intermediate or final product disclosed in Hayashi et al. which represents a phosphine chloride).

As discussed earlier, with regard to a Grignard reaction, the method of Berlin et al. lacks motivation due to the mentioned yields for the Grignard reaction in comparison with the disclosed Michaelis-Arbuzov rearrangement. If the teaching is nevertheless applied and combined with the teaching of Hayashi et al., there is still a lack of the appropriate substrate from the teaching of Hayashi et al., as there is no such necessary phosphine chloride.

Further, while the substrate in the disclosure of Berlin et al. contains a P-Cl bonding, it should be noted that it is still a P(V)-compound instead of a P(III)-compound and that the compound obtained from the "serious side reaction" is still not a chiral phosphine due to the presence of two equal radicals R (= phenyl groups), which is in contrast to the instant reaction, which leads to a chiral phosphine.

Further, the argumentation by the Examiner so far lacks any reasoning why the result(s) of the combined teachings is(are) obvious. With "result" is meant the finding that the inventive process leads to the formation of primarily one of more than one possible diastereomers.

Even assuming that there would be motivation from the teaching of Nettekoven et al. to search for an alternative preparation process for chiral phosphine ligands with the intention that only one diastereomer, or at least primarily only one diastereomer would be obtained, there is nothing to be found in the teachings of Hayashi et al. and Berlin et al. which could give rise for such an expectation.

Thus, even if Berlin et al. do not teach away from the Grignard reaction as argued by the Examiner, the result of combining the references would still not lead to the presently claimed invention for the reasons discussed above.

Accordingly, Applicants maintain their position that the present invention is not obvious from the references, and that the rejection of the claims under 35 U.S.C. §103(a) should be withdrawn, placing the application in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Wei-Ping CHEN et al.

By



Michael R. Davis

Registration No. 25,134

Attorney for Applicants

MRD/pth  
Washington, D.C. 20005-1503  
Telephone (202) 721-8200  
Facsimile (202) 721-8250  
May 3, 2010